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AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599

EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,189	IANNOTTI ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 24-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 24-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 3 August 2007 in which claims 5 and 9 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The interview summary is acknowledged and the interview record is complete.

The objections to the claims listed in the previous Office Action are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-9 and 24-37 are under prosecution.

Information Disclosure Statement

2. The Information Disclosure Statement filed 13 September 2007 is acknowledged. However, only the Abstract of Documents DE 197 46 874 and DE 200 03 081 are being considered because English language translations of the remainder of the documents have not been provided. The European Search Report has been considered but has been lined through because there is no publication date. See 37 CFR 1.98.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996) and in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)).

Regarding claim 1, Qiagen teaches a method of preparing a sample substantially free of genomic DNA. In a single exemplary embodiment, Qiagen teaches forming a lysate from liver cells (page 31, steps 1-2). The lysate contains genomic DNA. Qiagen further teaches contacting a pre-filtration column with said lysate; namely, the lysate is contacted with a Qiagen-tip (page 31, step 9), which is a column comprising a filter material in the form of a resin (page 3). Genomic DNA binds to said filter material (page 4, last paragraph and Table 1 on page 5). A first effluent comprising total RNA; namely, buffer

QRU elutes the RNA (page 31, step 12). Buffer QRU does not have enough NaCl to elute the genomic DNA from the column (Page 33 and Table 1 on page 5); thus, the first effluent is substantially free of genomic DNA.

Qiagen also teaches the column comprises a frit (page 11, third paragraph). A frit is a layer. Webster's defines a frit as comprising glass (page 912); thus, Qiagen teaches a glass layer in the form of a frit.

Qiagen does not teach contacting a second column with the first effluent. Thus, Qiagen teaches the method purifies RNA and genomic DNA is retained on the pre-filtration column in a base method that differs from the instantly claimed method because Qiagen does not teach a second column.

However, Avjioglu et al teach a method of preparing a sample substantially free of genomic DNA in the form of a method for purification and separation of mRNA (; column 14, line 35-column 15, line 10). Avjioglu et al teach collecting an effluent from a prefiltration column run with a lysate and subjecting the effluent to a second column (column 14, line 35-column 15, line 10). Avjioglu et al also teach the second column has the added advantage of increasing the purity of the sample to over 90% (column 15, lines 1-10). Thus, Avjioglu et al teach the known technique of using a second column in the purification of RNA.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Qiagen with the second column of Avjioglu et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of increasing the purity of the sample to over 90% as explicitly taught by Avjioglu et al (column 15, lines 1-10). In addition, it would have been obvious to the ordinary artisan that the known technique of using the second column of Avjioglu et al could have been applied to the method of Qiagen with predictable results because the second column of Avjioglu et al predictably results in further purification of the RNA sample.

Neither Qiagen nor Avjioglu et al teach silicon carbide whisker columns. Thus, Qiagen in view of Avjioglu et al teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al do not teach silicon carbide columns.

However, Haj-Ahmad teaches a method of isolating a nucleic acid from a sample matrix comprising contacting a silicon carbide column with said sample preparation (column 3, lines 38-41), and eluting said nucleic from said silicon carbide column (column 3, lines 41-55) with the added benefit that silicon carbide is an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids (column 2, lines 30-35). Thus, Haj-Ahmad teach the known technique of using a silicon carbide column in the purification of RNA.

While Haj-Ahmad also teaches the preferred embodiment wherein the silicon carbide has an average particle size of 4.5 microns (column 4, lines 1-3), neither Qiagen, Avjioglu, nor Haj-Ahmad specifically teach silicon carbide whiskers. However, the specification does not define what is encompassed by the term "whisker." The term "whisker" has therefore been interpreted to be encompassed by the preferred embodiment of Haj-Ahmad, wherein the silicon carbide particles have an average particle size of 4.5 microns (column 4, lines 1-3). Thus, the claim has been given the broadest reasonable interpretation consistent with the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]).

In addition, the courts have held that "where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device." (*Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), (see MPEP 2144.04, IVA). In the event that the instantly claimed "whiskers" are not encompassed by the micron sized particles of Haj-Ahmad, the instantly claimed "whiskers" would therefore merely be a form of silicon carbide having different relative

dimensions than those of the prior art, and as such are not patentably distinct from the particles of Haj-Ahmad.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a second column as taught by Qiagen in view of Avjioglu et al by using a silicon carbide column as taught by Haj-Ahmad with a reasonable expectation of success. The modification would result in the use of a silicon carbide whisker column as the second column in the method. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column composed of an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids as explicitly taught by Haj-Ahmad (column 2, lines 30-35). In addition, it would have been obvious to the ordinary artisan that the known technique of using the silicon carbide column of Haj-Ahmad could have been applied to the method of Qiagen in view of Avjioglu et al with predictable results because the silicon carbide column of Haj-Ahmad predictably results in purification of the RNA sample.

Regarding claims 2-4, the method of claim 1 is discussed above. Qiagen further teaches the lysate is formed using a lysis buffer having a chaotropic agent; namely, solutions R1-R4 are added to homogenize and lyse the sample, wherein the buffers comprise 4M guanidine isothiocyanate (i.e., claims 3-4; pages 31 and 33). Guanidine isothiocyanate is a chaotropic agent (i.e., claim 2).

Regarding claims 5-6, the method of claim 1 is discussed above. Qiagen also teaches the biological sample is a lysate from liver cells (page 31, steps 1-2), which are organ extracts of animal cells.

Response to Arguments

Applicant's arguments filed 3 August 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on page 7 of the Remarks that the method described by Qiagen is a method for the purification of DNA.

However, the cited pages of Qiagen (i.e., page 31) is specifically directed to isolation of RNA from a liver lysate using a column (first line). In addition, as noted above, the nucleic acid solution is suspended in 8 mL of buffer R5 and 2 ml of buffer R6, which results in a total salt concentration of 0.4M (steps 7-9). The solution is then loaded onto the QIAGEN-tip column, and eluted with buffer QA (steps 10-11), which also has 0.4 M salt (i.e., NaCl). Table 1 on page 5 clearly indicates that large DNA, in the form of plasmid and lambda DNA, do not elute from the column at such low salt concentrations. Genomic DNA, which is larger than plasmid DNA, would similarly be retained. Thus, Qiagen teaches the method purifies RNA and genomic DNA is retained on the pre-filtration column.

B. Applicant also argues on page 7 of the Remarks that Qiagen does not teach the use of a glass or borosilicate filter to bind genomic DNA.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., use of a glass or borosilicate filter to bind genomic DNA) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claim requires that the filter material has at least one layer of glass or borosilicate fiber and that genomic DNA is bound by the filter material, but does not necessarily bind to the glass or borosilicate fiber as long as the genomic DNA binds to the remainder of the filter material.

C. Applicant further argues on page 7 of the Remarks that a filter is not necessary because the anionic resin binds the DNA.

Applicant's argument has been considered but is moot because Qiagen teaches said filter in the form of a frit in the column (page 11, third paragraph). A frit is a layer. Webster's defines a frit as

comprising glass (page 912); thus, Qiagen teaches a the required element of a glass layer in the form of a frit.

D. Applicant argues on page 7 of the Remarks that the '972 patent of Avjioglu et al does not teach a prefiltration column comprising a glass or borosilicate filter, collecting the effluent, or contacting the effluent with a silicon carbide whisker column.

However, contrary to Applicant's argument, Avjioglu et al explicitly teach collecting an effluent from a prefiltration column run with a lysate and subjecting the effluent to a second column (column 14, line 35-column 15, line 10). The prior art of Avjioglu et al is solely relied upon for the teaching of running a second column after RNA has been separated from a lysate; i.e., purified to be substantially free of genomic DNA, which has the added advantage of increasing the purity of the sample to over 90% (column 15, lines 1-10).

E. Applicant further argues on page 7 of the Remarks that the '278 patent of Haj-Ahmad does not teach a prefiltration column comprising a glass or borosilicate filter that binds genomic DNA.

However, the prior art of Haj-Ahmad is solely relied upon for the teaching that nucleic acids can be purified using silicon carbide columns (column 3, lines 41-55) with the added benefit that silicon carbide is an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids (column 2, lines 30-35). Thus, Haj-Ahmad provides motivation for using a silicon carbide column as the second column suggested by Avjioglu et al.

F. In response to applicant's argument on page 8 of the Remarks that that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Qiagen teaches clearly indicates in Table 1 on page 5 that large DNA, in the form of plasmid and lambda

DNA, do not elute from the column at such low salt concentrations. Genomic DNA, which is larger than plasmid DNA, would similarly be retained. Thus, Qiagen teaches the method purifies RNA and genomic DNA is retained on the pre-filtration column in a base method that differs from the instantly claimed method because Qiagen does not teach a second column.

Avjioglu et al explicitly teach collecting an effluent from a prefiltration column run with a lysate and subjecting the effluent to a second column (column 14, line 35-column 15, line 10). The prior art of Avjioglu et al is solely relied upon for the teaching of running a second column after RNA has been separated from a lysate; i.e., purified to be substantially free of genomic DNA, which has the added advantage of increasing the purity of the sample to over 90% (column 15, lines 1-10). Thus, Avjioglu et al teach the known technique of using a second column in the purification of RNA.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Qiagen with the second column of Avjioglu et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of increasing the purity of the sample to over 90% as explicitly taught by Avjioglu et al (column 15, lines 1-10). In addition, it would have been obvious to the ordinary artisan that the known technique of using the second column of Avjioglu et al could have been applied to the method of Qiagen with predictable results because the second column of Avjioglu et al predictably results in further purification of the RNA sample.

Thus, Qiagen in view of Avjioglu et al teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al do not teach silicon carbide columns.

However, Haj-Ahmad teaches a method of isolating a nucleic acid from a sample matrix comprising contacting a silicon carbide column with said sample preparation (column 3, lines 38-41), and eluting said nucleic from said silicon carbide column (column 3, lines 41-55) with the added benefit that silicon carbide is an affordable and readily available substance available in a variety of grades, each grade

having a different capacity for binding nucleic acids (column 2, lines 30-35). Thus, Haj-Ahmad teach the known technique of using a silicon carbide column in the purification of RNA.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a second column as taught by Qiagen in view of Avjioglu et al by using a silicon carbide column as taught by Haj-Ahmad with a reasonable expectation of success. The modification would result in the second column being a silicon carbide whisker column. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column composed of an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids as explicitly taught by Haj-Ahmad (column 2, lines 30-35). In addition, it would have been obvious to the ordinary artisan that the known technique of using the silicon carbide column of Haj-Ahmad could have been applied to the method of Qiagen in view of Avjioglu et al with predictable results because the silicon carbide column of Haj-Ahmad predictably results in purification of the RNA sample.

6. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996) and in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)) as applied to claim 1 above, and further in view of Poad (U.S. Patent No 3,414,394, issued 3 December 1996).

Regarding claim 7, the method of claim 1 is discussed above in Section 5. Neither Qiagen, Avjioglu, nor Haj-Ahmad et al teach the filter material (i.e., the frit) has a particle retention (i.e., pore size) from about 0.1 to about 10 microns. Thus, Qiagen in view of Avjioglu et al in view of Haj-Ahmad teach a

base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al in view of Haj-Ahmad do not teach the pore sizes of the instant claims.

However, Poad teaches frits having pore sizes of about 2.4 microns (column 2, lines 20-30) having the added advantage of having both high strength and high permeability (column 1, lines 55-59). High permeability decreases the time required to run the column. Thus, Poad teaches the known technique of using pore sizes of the instant claims.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a fritted column as taught by Qiagen in view of Avjioglu et al in view of Haj-Ahmad with the filter material having the pore size as taught by Poad with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column having both high strength and decreased running times as explicitly taught by Poad (column 1, lines 55-59). In addition, it would have been obvious to the ordinary artisan that the known technique of using the pore sizes of Poad could have been applied to the method of Qiagen in view of Avjioglu et al in view of Haj-Ahmad with predictable results because the pore sizes of Poad predictably results in frits useable as filters.

7. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996) and in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)) as applied to claim 1 above, and further in view of Colpan et al (U.S. Patent No. 6,383,393 B1, issued 7 May 2002).

Regarding claim 8, the method of claim 1 is discussed above in Section 5. Neither Qiagen, Avjioglu, nor Haj-Ahmad et al explicitly teach the filter material is about 50 to about 2000 microns thick.

Thus, Qiagen in view of Avjioglu et al in view of Haj-Ahmad teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al in view of Haj-Ahmad do not teach the thickness of the instant claims.

However, Colpan et al teach the use of pre-filtration columns comprising at least one layer of glass in the filter material (column 7, lines 30-36), wherein the glass layer has fibers having a thickness (i.e., length) of about 300 microns (column 7, lines 30-32). Colpan et al also teach the glass fibers have the added advantage of allowing quantitative, specific, and reversible binding of the nucleic acid sample to the fibers (column 4, lines 53-60). Thus, Colpan et al teach the known technique of using the thickness of the instant claims.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Qiagen in view of Avjioglu et al in view of Haj-Ahmad with the filter material having the thickness as taught by Colpan et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column having the added advantage of allowing quantitative, specific, and reversible binding of the nucleic acid sample to the fibers as explicitly taught by Colpan et al (column 1, lines 55-59). In addition, it would have been obvious to the ordinary artisan that the known technique of using the thickness of Colpan et al could have been applied to the method of Qiagen in view of Avjioglu et al in view of Haj-Ahmad with predictable results because the thickness of Colpan et al predictably results in glass layers usable in the purification of nucleic acids.

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996) and in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)) as applied to claim 1 above, and further in view of the Aldrich Catalog (Aldrich Chemical Company, Milwaukee, WI, page T289 (1998/1999)).

Regarding claim 9, the method of claim 1 is discussed above in Section 5 . Neither Qiagen, Avjioglu et al, nor Haj-Ahmad teach the weight of the glass filters. Thus, Qiagen in view of Avjioglu et al in view of Haj-Ahmad teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al in view of Haj-Ahmad do not teach the weight of the instant claims.

However, Aldrich teaches glass fibers suitable for use in chromatography that are 2 in diameter bundles that are 22 feet long, weighing 454 g (page T281, column 2, paragraph 1). A filter layer having a 2 in (5.08 cm) diameter has an area of 0.00203 m^2; therefore, a filter layer having a 2 in diameter and a length (i.e., the thickness of the layer in a column) of 0.25 in has a specific weight of 212 g/m^2, thereby meeting the limitation of the claim. Aldrich also teaches the glass fibers are strong and free of heavy metals (page T281, column 2, paragraph 1). Thus, Aldrich teaches the known technique of using the weight of the instant claims.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method as taught by Qiagen in view of Avjioglu et al in view of Haj-Ahmad with the filter material having the specific weight as taught by Aldrich with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column having a glass layer having the added advantages of strength and freedom from heavy metal contaminants as explicitly taught by Aldrich (page T281, column 2, paragraph 1). In addition, it would have been obvious to the ordinary artisan that the known technique of using the weight of Aldrich could have been applied to the

method of Qiagen in view of Avjioglu et al in view of Haj-Ahmad with predictable results because the weight of Aldrich predictably results in a glass layer useable in the chromatographic purification operations.

9. Claims 24-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996), in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), and in view of Dove et al (U.S. Patent No. 5,006,472, issued 9 April 1991), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)).

Regarding claims 24 and 26, Qiagen teaches a method of preparing a sample substantially free of genomic DNA. In a single exemplary embodiment, Qiagen teaches forming a lysate (page 31, steps 1-2). The lysate contains genomic DNA. Qiagen further teaches contacting a pre-filtration column with aid lysate; namely, the lysate is contacted with a Qiagen-tip (page 31, step 9), which is a column comprising a filter material in the form of a resin (page 3). Genomic DNA binds to said filter material (page 4, last paragraph and Table 1 on page 5). A first effluent comprising total RNA; namely, buffer QRU elutes the RNA (page 31, step 12). Buffer QRU does not have enough NaCl to elute the genomic DNA from the column (Page 33 and Table 1 on page 5); thus, the first effluent is substantially free of genomic DNA.

Qiagen also teaches the column comprises a frit (page 11, third paragraph). A frit is a layer. Webster's defines a frit as comprising glass (page 912); thus, Qiagen teaches a glass layer in the form of a frit.

Qiagen does not teach contacting a second column with the first effluent. Thus, Qiagen teaches the method purifies RNA and genomic DNA is retained on the pre-filtration column in a base method that differs from the instantly claimed method because Qiagen does not teach a second column.

However, Avjioglu et al teach a method of preparing a sample substantially free of genomic DNA in the form of a method for purification and separation of mRNA (; column 14, line 35-column 15, line 10). Avjioglu et al teach collecting an effluent from a prefiltration column run with a lysate and subjecting the effluent to a second column (column 14, line 35-column 15, line 10). Avjioglu et al also teach the second column has the added advantage of increasing the purity of the sample to over 90% (column 15, lines 1-10). Thus, Avjioglu et al teach the known technique of using a second column in the purification of RNA.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of Qiagen with the second column of Avjioglu et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of increasing the purity of the sample to over 90% as explicitly taught by Avjioglu et al (column 15, lines 1-10). In addition, it would have been obvious to the ordinary artisan that the known technique of using the second column of Avjioglu et al could have been applied to the method of Qiagen with predictable results because the second column of Avjioglu et al predictably results in further purification of the RNA sample.

Neither Qiagen nor Avjioglu et al teach silicon carbide whisker columns. Thus, Qiagen in view of Avjioglu et al teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al do not teach silicon carbide columns.

However, Haj-Ahmad teaches a method of isolating a nucleic acid from a sample matrix comprising contacting a silicon carbide column with said sample preparation (column 3, lines 38-41), and eluting said nucleic from said silicon carbide column (column 3, lines 41-55) with the added benefit that silicon carbide is an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids (column 2, lines 30-35). Thus, Haj-Ahmad teach the known technique of using a silicon carbide column in the purification of RNA.

While Haj-Ahmad also teaches the preferred embodiment wherein the silicon carbide has an average particle size of 4.5 microns (column 4, lines 1-3), neither Qiagen, Avjioglu, nor Haj-Ahmad specifically teach silicon carbide whiskers. However, the specification does not define what is encompassed by the term "whisker." The term "whisker" has therefore been interpreted to be encompassed by the preferred embodiment of Haj-Ahmad, wherein the silicon carbide particles have an average particle size of 4.5 microns (column 4, lines 1-3). Thus, the claim has been given the broadest reasonable interpretation consistent with the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]).

In addition, the courts have held that "where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device." (*Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), (see MPEP 2144.04, IVA). In the event that the instantly claimed "whiskers" are not encompassed by the micron sized particles of Haj-Ahmad, the instantly claimed "whiskers" would therefore merely be a form of silicon carbide having different relative dimensions than those of the prior art, and as such are not patentably distinct from the particles of Haj-Ahmad.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising a second column as taught by Qiagen in view of Avjioglu et al by using a silicon carbide column as taught by Haj-Ahmad with a reasonable expectation of success. The modification would result in the use of a silicon carbide whisker column as the second column. The ordinary artisan would have been motivated to make the modification because the modification would have resulted in method having a column composed of an affordable and readily available substance available in a variety of grades, each grade having a different capacity for binding nucleic acids as explicitly taught by Haj-Ahmad (column 2, lines 30-35). In addition,

it would have been obvious to the ordinary artisan that the known technique of using the silicon carbide column of Haj-Ahmad could have been applied to the method of Qiagen in view of Avjioglu et al with predictable results because the silicon carbide column of Haj-Ahmad predictably results in purification of the RNA sample.

Neither Qiagen, Avjioglu et al, nor Haj-Ahmad teach DNAse. Thus, Qiagen in view of Avjioglu et al in view of Haj-Ahmad teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al in view of Haj-Ahmad do not teach digestion with DNAse (i.e., claims 24 and 26).

However, Dove et al teach a method of preparing a sample via a purification process using enzymatic treatment (Abstract) comprising contacting nucleic acids bound to a column with DNAse, under conditions suitable for DNAse digestion; namely, DNA is degraded when it is bound by DNAse that is immobilized on a column (column 3, lines 20-24); therefore, when the DNA is bound to the immobilized DNAse, the DNA is bound to the column and contacts the DNAse. Dove et al also teach the added advantage that the treatment on the column results in the degradation of undesirable residual nucleic acids (Abstract). Thus, Dove et al teach the known technique of using DNAse during purification of nucleic acids.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the columns as taught by Qiagen in view of Avjioglu et al in view of Haj-Ahmad with the columns comprising DNAse as taught by Dove et al with a reasonable expectation of success. The modification taught by Dove et al would result in including DNA digestion during the collection of the effluent from the pre-filtration column (i.e., claim 26) as well as DNA digestion during the contacting with the silicon carbide column (i.e., claim 24). The ordinary artisan would have been motivated to make the modification because the modification would have resulted in a method having the added advantage of allowing the degradation of undesirable residual nucleic acids on each of the two columns as explicitly taught by Dove et al (Abstract). In addition, it would have been

obvious to the ordinary artisan that the known technique of using the DNAse Dove et al of could have been applied to the method of Qiagen in view of Avjioglu et al in view of Haj-Ahmad with predictable results because the DNAse of Dove et al predictably results degradation of DNA contaminants in the RNA sample.

Regarding claim 25 , the method of claim 24 is discussed above. Qiagen further teaches the nucleic acid is RNA; namely, the method is specifically directed to isolation of RNA from a liver lysate using a column (page 31, first line).

Regarding claims 27-29, the method of claim 24 is discussed above. Qiagen further teaches the lysate is formed using a lysis buffer having a chaotropic agent; namely, solutions R1-R4 are added to homogenize and lyse the sample, wherein the buffers comprise 4M guanidine isothiocyanate (i.e., claims 28-29; pages 31 and 33). Guanidine isothiocyanate is a chaotropic agent (i.e., claim 27).

Regarding claims 30-31, the method of claim 24 is discussed above. While Qiagen do not explicitly teach organic solvents in the lysis step, Qiagen does teach organic solvents in the form of ethanol (i.e., claim 31) are added to the lysate. The courts have held that selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). Thus, the addition of organic solvents during the lysis step is obvious over the later addition of organic solvents as taught by Qiagen. See MPEP 2144.04 IV.C.

Regarding claim 32, the method of claim 24 is discussed above. Qiagen also teaches the column comprises a frit (page 11, third paragraph). Thus, the modification of the method of Qiagen in view of Avjioglu et al with the silicon carbide column of Haj-Ahmad et al would result in a second column having a frit with the silicon carbide whiskers adjacent to said frit.

Regarding claims 33-36, the method of claim 24 is discussed above. Qiagen further teaches the lysate is formed using solutions R1-R6, which are added to homogenize and lyse the sample. The buffers comprise beta-mercaptoethanol (i.e., claim 33), a pH of about 4 to about 8 (i.e., claim 34; pages 31 and 33). Qiagen also teaches RNA buffers are treated with DEPC to make them ribonuclease free (i.e., claim 35;

page 9, last paragraph). The sample is eluted with buffer QRU, which has a pH of about 6 to about 9 (i.e., claim 36; page 31, step 12).

10. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Qiagen (The Qiagenologist Application Protocols, 3rd edition, Qiagen Inc., Chatsworth, CA, pages 2-11 and 30-37 (1990)) in view of Avjioglu et al (U.S. Patent No. 5,480,972, issued 2 January 1996), in view of Haj-Ahmad (U.S. Patent 6,177,278, issued 23 January 2001), in view of Dove et al (U.S. Patent No. 5,006,472, issued 9 April 1991), as defined by Webster (Webster's Third New International Dictionary, Miriam-Webster Inc., USA, page 91 (1963)), as applied to claim 24 above, and further in view of Crossway et al (U.S. Patent No. 4,996,144, issued 26 February 1991).

Regarding claim 37, the method of claim 24 is discussed above in Section 9. Neither Qiagen, Avjioglu et al, Haj-Ahmad, nor Dove et al teach additional digestion with DNAse. Thus, Qiagen in view of Avjioglu et al in view of Haj-Ahmad in view of Dove et al teach a base method that differs from the instantly claimed method because Qiagen in view of Avjioglu et al in view of Haj-Ahmad in view of Dove et al do not teach additional digestion with DNAse.

However, Crossway et al teach a method of purification of nucleic acids (e.g., RNA; Abstract, lines 3-5) using additional digestion with DNAse with the added benefit of allowing differential detection of RNA only (column 5, lines 60-63). Thus, Crossway et al teach the known technique of using additional digestion with DNAse.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method of isolating a nucleic acid as taught by Qiagen, Avjioglu et al, Haj-Ahmad, and Dove et al with the additional DNAse treatment as taught by Crossway et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in a method having the added advantage of allowing differential detection of RNA only as explicitly taught by Crossway et al (column

5, lines 60-63). In addition, it would have been obvious to the ordinary artisan that the known technique of using the additional digestion with DNAse of Crossway et al could have been applied to the method of Qiagen in view of Avjioglu et al in view of Haj-Ahmad in view of Dove et al with predictable results because the additional digestion with DNAse of Crossway et al predictably results in removal of DNA contaminants of an RNA sample.

Response to Arguments

The remaining arguments on pages 8-11 of the Remarks rely on arguments set forth to address the rejections of claims 1-6 under 35 USC 103(a). Since the arguments regarding claims 1-6 were not persuasive, the rejections of the dependent claims are maintained.

Conclusion

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

13. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jehanne Sitton/
Primary Examiner
9/26/2007

Robert T. Crow
Examiner
Art Unit 1634